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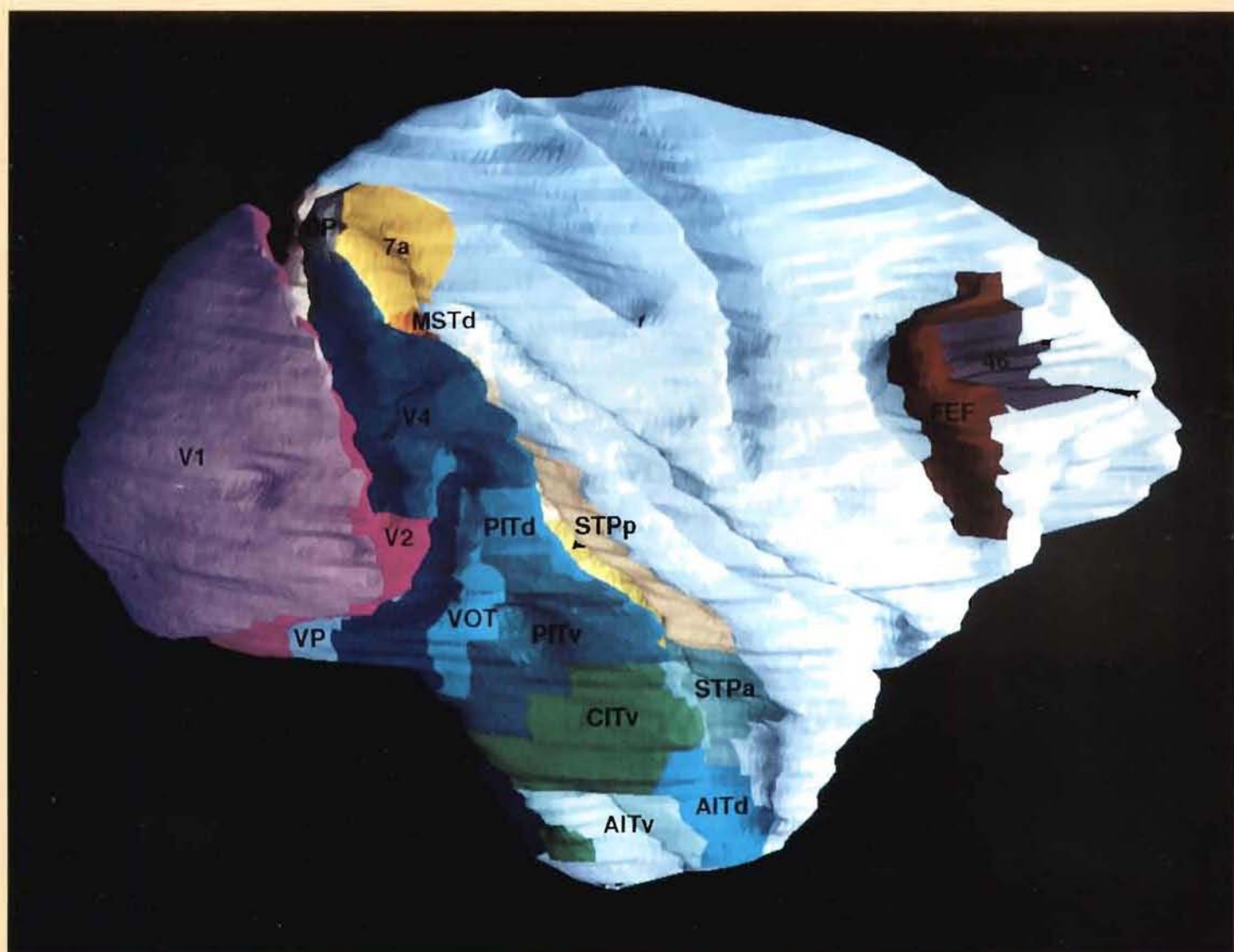
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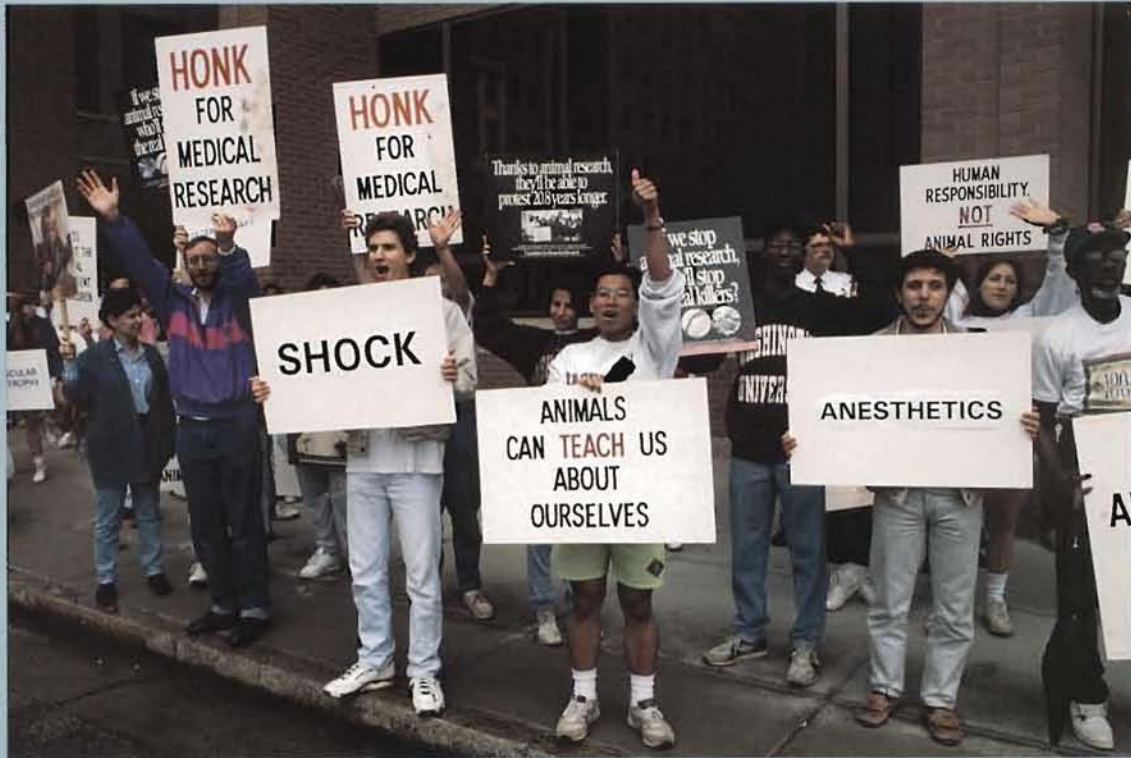
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OUTLOOK



**Processing
Visual Information**



At a demonstration organized by animal rights activists on May 1, supporters of humane and ethical animal research outnumbered their opponents. Supporters of animal research carried signs to remind the public of the many conditions that animal research has helped medical science to understand and control. The demonstrations, held at the Medical Center, were vocal but peaceful.

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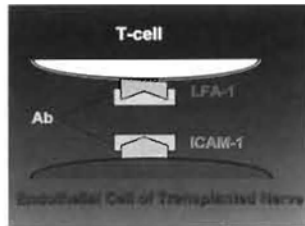
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On The Cover:

A computer-generated view of the macaque visual system; structures related to vision are depicted in color. Research under the direction of David C. Van Essen, Ph.D., head of the Department of Anatomy and Neurobiology, explores information processing in the primate's visual system. Photograph by Tom Heine. Story on page 12.



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Workshops Spread The Word

In mid-May, David Schlessinger, Ph.D., and his colleagues in St. Louis hosted nearly 100 scientists at the international 4th X Chromosome Workshop.

From around the world, researchers with interests in the human X chromosome gathered at the Ritz-Carlton Hotel in Clayton to exchange information, visit computer demonstrations, view poster sessions and hear more formal presentations.

In addition, a huge bulletin board carried a likeness of the X chromosome, and researchers were encouraged

to fill in the blanks with information they had discerned in their investigations. The St. Louis group, one of the world's most active, added contributions that have helped to organize more than 80 percent of the chromosome into mapped regions.

A week after the X chromosome workshop, Eric D. Green, M.D., Ph.D., was in Marburg, Germany, helping to chair the first workshop for researchers studying human chromosome 7.

Along with co-organizers from Canada and Germany, Green hosted 50 researchers from around the world. The group shared information concerning the techniques their labs employ to map the chromosome, the maps they have produced and the reagents that they use. ■

Study Defines Cause Of Diabetes Subtype

Researchers here have identified 16 gene mutations responsible for causing a subform of adult-onset diabetes. The study provides the most complete explanation to date of the cause of any form of diabetes and is the most thorough investigation of any gene's role in the disease.

"For the first time we clearly know the cause of diabetes in a subset of these patients," says Alan Permutt, M.D., professor of medicine. Permutt's laboratory conducted the study with collaborators from the University of Chicago and the Centre d'Etude Polymorphisme Humain in Paris. Genetic discoveries such as these may eventually lead to gene therapies and to genetic tests that predict diabetes in non-symptomatic people, he adds.

The researchers looked for mutations in the gene for glucokinase, an enzyme thought to be critical for stimulating pancreatic insulin secretion. A few mutations in this gene have been reported in past studies, Permutt explains, but were found in only four families. This study looked at a large group of diabetic families to find a more definitive explanation of the role glucokinase mutations play in the development of adult-onset

diabetes, also called Type II diabetes.

Using DNA isolated from blood cells, the investigators studied 53 French families — 21 with Type II diabetes and 32 with a Type II subform called maturity-onset diabetes of the young (MODY), Permutt says. Type II diabetes is the most common form of the disease and affects about 12.5 million Americans. It normally appears in middle age and is characterized by the inability to produce enough insulin or to respond properly to insulin. MODY is a subform in which symptoms appear before age 25. It accounts for about five percent of Type II cases.

Researchers found 16 mutations in 18 (56 percent) of the MODY families and no mutations in any of the other families. In addition, they found that patients with glucokinase mutations were diagnosed earlier in childhood and were more mildly affected than MODY patients with normal glucokinase genes. Their findings imply that — at least in this study population — the glucokinase gene is the primary cause of MODY and probably does not play an important role in causing non-MODY cases of Type II diabetes.

Although it is likely that similar mutations will be



David Schlessinger, Ph.D., and research associate Gina Pengue examine one of the postings at the recent 4th X Chromosome Workshop, held in St. Louis.

found in other racial and ethnic groups, additional studies will be needed to clarify the glucokinase gene's role outside of this study population, Permutt cautions. He currently is studying the glucokinase gene in African Americans and Mauritian Creoles. In addition to glucokinase mutations, genetic studies have linked MODY diabetes to an unknown gene on chromosome 20, Permutt says. ■

Malaria Parasite's Feeding Tube Found

Researchers have found a molecular "feeding tube" that may be critical to the malaria parasite's survival in human red blood cells. The molecule is an ion channel that

allows essential nutrients to pass from the red blood cell into the parasite, investigators report.

"This seems to be a molecule that is involved in the parasite's eating behavior, and it may be necessary for the parasite to live. So eventually it could be a target for the development of drugs to starve malaria," says Edwin McCleskey, Ph.D., associate professor of cell biology and physiology.

The malaria parasite spends part of its complex life cycle inside human red blood cells, McCleskey explains. There, it exists encased in two membranes: One is its own, and the other is a sac formed around the parasite from the red blood cell's membrane. The parasite multiplies inside the red cell for two days, then bursts out, sending roughly 32 new parasites into the blood to infect 32 more red cells.

While in red cells, the organism uses hemoglobin

as its main food source. "But it also needs glucose and some amino acids that are not present in hemoglobin. So it has to come up with ways to get these foods, and everything it eats has to come through the red blood cell," McCleskey says. Until now, there was no explanation for how such nutrients actually crossed the double barrier.

The investigators found several unusual characteristics of the new channel that suggest it plays a role in feeding, he says. Typically, ion channels are extremely selective; they allow only very small particles of a certain charge to pass through. But the parasite's channels are permeable to both positive and negative ions, as well as organic molecules too large to pass through most channels, the investigators found.

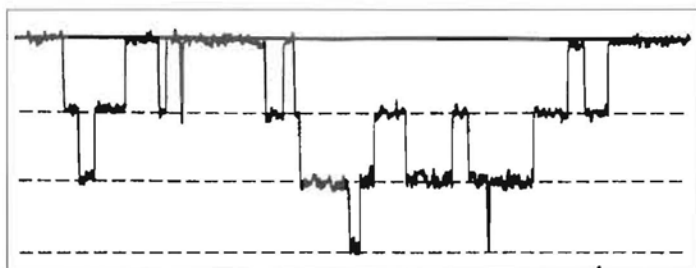
The next step, McCleskey says, is to find an easier way to study the channel. Studies to understand the biology of the malaria parasite are essential because 5,000 people a day die from the disease worldwide, McCleskey says. Most deaths result from one parasite species that is resistant to the most important malarial drug, chloroquine. "So we do need additional drugs or a vaccine. We try to describe the biology of the parasite to find molecules that are essential for it to live and then design drugs to knock those molecules out," McCleskey says. ■

Perlmutter Named Scholar

The Burroughs Wellcome Fund has named David H. Perlmutter, M.D., one of two recipients of the Experimental Therapeutics Scholar Award for 1993. The awards of \$350,000, payable over five years, encourage the development of outstanding clinical scientists dedicated to closing the gap between the basic sciences and their application to clinical medicine.

The award is for work in the Perlmutter laboratory showing that a specific cell surface receptor for alpha-1-antitrypsin-protease complexes, the SEC receptor, also recognizes the beta-amyloid peptide. The beta-amyloid peptide accumulates in the brains of patients with Alzheimer's disease and has been linked to dementia in those patients. The SEC receptor may therefore be an excellent target of novel pharmacologic approaches for treatment of Alzheimer's.

Perlmutter's lab also studies the biochemistry of a genetic deficiency of alpha-1-antitrypsin, the most common metabolic cause of liver disease in infants and the most common metabolic cause of emphysema in adults. ■



In this oscilloscope tracing, each downward deflection from the topmost horizontal represents the opening of a single ion-channel feeding tube in a malaria parasite. Three feeding tubes have been isolated, each capable of transporting a million ions per second. The activity is determined electrically, with the difference between open and closed equal to about 5×10^{-12} amps. One amp is roughly equal to the current required by a light bulb.

Abdominal Obesity Linked To Diabetes

Abdominal obesity appears to be a stronger factor than age in the development of adult-onset diabetes in older adults, according to researchers here.

Investigators studied 67 men and women aged 60 to 70 to find out whether aging

lin, the hormone responsible for lowering blood sugar levels.

Subjects were evaluated for body fat distribution, level of physical fitness, glucose tolerance and insulin resistance. Forty-three subjects who had varying degrees of insulin resistance

ratio — did not explain the inability to regulate blood sugar level.

“Basically, if we take any measurements in the trunk region, those who have impaired glucose tolerance and insulin resistance tend to show more central adiposity (fat),” says Wendy M. Kohrt, Ph.D., research assistant professor and principal investigator. “We found the same held true in both men and women.”

Blood glucose levels are held in check by insulin, the hormone secreted by the body to clear glucose from the blood into muscles, where it is stored for energy. With advancing age, Kohrt says, insulin produced isn’t as effective in controlling blood sugar. To offset higher sugar levels, the body often compensates by secreting more insulin. As a result, Kohrt says, many older people with high blood sugar levels also have high insulin levels that can make them insulin resistant and lead to non-insulin-dependent, or adult-onset, diabetes mellitus.

“Our study cannot rule out the possibility that there is a decline in glucose tolerance associated with the aging process,” says Kohrt. “It does suggest, however, that many of the changes that have been attributed to aging are the result of changes in regional adiposity, which is probably secondary to the

decline in physical activity that frequently accompanies aging. The good news is that it’s something that is very amenable to change through modest dieting and exercise.” ■

Foundation Supports Training PET Experts

As part of the Dana Foundation’s recently announced \$25 million commitment to a consortium on memory loss and aging, physicians here and at UCLA have been named to train a cadre of specialists in positron emission tomography (PET) imaging of the human brain.

The foundation is bringing advances in neuroscience to an understanding of the brain and the treatment of brain-related diseases. PET will play a key role in advancing understanding of the biology of the brain by allowing noninvasive imaging of healthy and diseased brains, making it possible to distinguish between healthy brain function and the metabolic impact that occurs as diseases interfere with normal brain function. Among the first research efforts supported by the foundation will be a focus on the biology of memory loss and aging.

Marcus E. Raichle, M.D., professor of neurology and of radiology, will coordinate



In a study of abdominal obesity and adult-onset diabetes, both men and women with insulin resistance were found to have increased central adiposity. Here, Wendy M. Kohrt, Ph.D., measures Benjamin Jenkins.

or belly fat is a bigger factor in the decline that occurs in the body’s ability to regulate blood sugar levels as age advances.

The inability to regulate blood sugar, known as glucose intolerance, develops when the body becomes resistant to the actions of insu-

were found to be significantly bigger around their chest, waist, and hips. Researchers found that when the effects of varying waist circumference were statistically controlled, other factors — such as age, fitness level, total body fat and the waist-to-hip circumference

the training of leaders in PET technology here under an initial grant of \$1.7 million. The grant can be expanded to a total of \$3 million over five years. PET, which images the body's functions rather than just its form, provides vivid pictures of reactions in the areas of the brain devoted to emotion, language and the forming and storing of memories. Developed at Washington University School of Medicine under the guidance of Michel M. Ter-Pogossian, Ph.D., PET continues to expand into new applications.

The Dana Foundation, founded in 1950, is a private philanthropic foundation with assets in excess of \$223 million. Among the foundation's commitments is the funding of research into brain-related disorders that affect millions. ■

Kipnis Named ACP Master

David H. Kipnis, M.D., Adolphus Busch Professor and former head of the Department of Internal Medicine, has been selected to become a Master of the American College of Physicians (ACP).

Masters are ACP fellows who — because of renown in medical practice or research, positions of honor and influence and personal character

— are recommended by the Awards, Masterships and Honorary Fellowships Committee to the ACP Board of Regents. Of the ACP's 75,000 members, only about 200 have achieved mastership. Kipnis joins Michael M. Karl, M.D., who became a Master in 1990. The late Carl V. Moore was the first Missouri physician to earn the honor.

Kipnis was head of the Department of Internal Medicine from 1973 until 1992. Regarded as a pioneer in diabetes research, Kipnis has worked to learn the mechanisms of sugar and amino acid transport and regulation of insulin released by islet cells in the pancreas. He pioneered the application of fundamental and biologic science to clinical situations.

Kipnis was deeply involved in the Washington University/Monsanto Biomedical Research agreement — the largest research collaboration between an American company and an American university. It has provided nearly \$100 million in research funding. Kipnis is also the chairman of the Scholar Advisory Committee of the Lucille P. Markey Charitable Trust.

The ACP is a non-profit organization of physicians trained in internal medicine. It includes practitioners providing primary care, medical specialists in cardiology, neurology and oncology, and medical researchers and teachers. ■

Olin Fellows Named, Donoghue Honored

Maria J. Donoghue has been selected as the first recipient of the Barbara Jakschik Award, to be presented annually to a senior female graduate student in recognition of outstanding academic and research accomplishments in the area of metabolic regulation. The award is named for Barbara Jakschik, Ph.D., who recently retired from the Department of Molecular Biology and Pharmacology.

Donoghue was among those selected as 1992 Spencer T. and Ann W. Olin Medical Scientist Fellows. Also named as fellows were: Stanley T. Carmichael, Jonathan N. Glickman, Howard P. Goodkin, Michelle L. Hermiston, Randall R. Johnson, Gregory

Joslin, Susan E. Koester, Brenda Myers-Powell, Thomas M. J. Niederman, David M. Pressel, Christopher R. Solaro, Joel S. Solomon, Thomas E. Wilson and John D. York.

Recognized for achievement in biomedical research, Olin Fellows look forward to outstanding careers in medically relevant areas of basic science. Most are pursuing combined M.D./Ph.D. degrees.

The fellowships are funded by a \$30 million commitment to the Division of Biology and Biomedical Sciences made in 1986 by the Spencer T. and Ann W. Olin Foundation. The gift supports students in the Medical Scientist Training Program (MSTP). ■



1992 Spencer T. and Ann W. Olin Medical Scientist Fellows (seated, left to right): Johnson, Pressel, Glickman, Solaro. (standing, left to right): Carmichael, Goodkin, Solomon, Hermiston, York, Donoghue, Niederman. Not pictured: Joslin, Koester, Myers-Powell and Wilson.

Anesthesiology Gets \$2 Million Program Project Grant

Three teams of investigators here will share a program project grant to fund studies of the mechanisms by which general anesthetics produce their effects. The grant is one of two awarded by the National Institutes of Health to investigate the cellular and molecular mechanisms by

well documented, no real agreement exists on why and how this class of drugs is able to make patients lose consciousness. The program director is Joseph H. Steinbach, Ph.D., professor of anesthesiology and of anatomy and neurobiology. He is also the principal investigator of one project that will study the ways in which anesthetics increase inhibition in individual cells in the brain.

Steinbach says, "We will be studying two different kinds of receptors in specific brain cells to see what it is that anesthetics actually do at the cellular and molecular level at clinically relevant doses."

The second project funded by the grant is an investigation of anesthetic drugs that are chemically larger than the gaseous anesthetics used in surgery. The structures of these drugs will be modified to learn more about the parts of molecules involved in producing anesthetic effects such as loss of consciousness. Douglas F. Covey, Ph.D., professor of molecular biology and pharmacology, is principal investigator. Charles F. Zorumski, M.D., associate professor of psychiatry and of anatomy and neurobiology, is co-investigator.

The third project will study the effects of anesthetics on calcium channels in

neurons. Christopher J. Lingle, Ph.D., associate professor of anesthesiology and of anatomy and neurobiology, will investigate the activation of calcium channels that is required for the transmission of information between nerve cells. Lingle will study the ways in which anesthetics inhibit calcium channels in specific types of nerve cells.

"The point of all three projects is to try to figure out what's going on," Steinbach says. "The goals are to clarify the molecular mechanisms by which anesthetics act and to determine whether one cellular or molecular action is clinically more relevant than another. In addition to increasing our understanding of the drugs in current use, the results could perhaps lead to the design of new approaches for producing anesthesia." ■

Alzheimer's Disease Research.

The Frank. H. Netter Lecture, sponsored by CIBA-Geigy, is awarded for excellence as a neuro-educator involved in clinically relevant research. Landau spoke on "The Practice of Clinical Neuroskepticism." His lecture was based on the illustrative case history of his own patient, whose fainting attack had been attributed to a condition known as carotid sinus syncope.

This stimulus led to critical review of the hospital record and 60 years of pertinent literature. By reasonable scientific standards, Landau maintained, neither the diagnosis nor the accepted understanding of the condition is valid. His advisory conclusion regarding neurological diagnosis was, quoting Finley Peter Dunne, "Trust everybody, but cut the cards."

Goate received the Potamkin Prize, which was established in 1988 to recognize "major contributions to the understanding of the causes and the prevention, treatment and ultimately the cure for Alzheimer's disease and related disorders." Goate is one of four recipients of this year's prize. The four will share a \$100,000 cash award.

Goate is internationally known for her discovery of a genetic mutation linked to cases of familial Alzheimer's disease. That discovery has been responsible for a world-



which anesthetics work and is worth more than \$2 million over five years, with the first year award totaling \$585,000.

Alex S. Evers, M.D., acting head of anesthesiology, calls the grant a recognition for groundbreaking research being conducted in the department. "Our efforts to better understand the ways in which anesthetics work are unique in the world today," Evers says.

Although the effectiveness of various anesthetics is

Landau, Goate Honored By Neurologists

William M. Landau, M.D., professor of neurology, and Alison M. Goate, D. Phil., associate professor of psychiatry and genetics, have been honored by the American Academy of Neurology. Landau delivered the 1993 Netter Lectureship and Goate was awarded the Potamkin Prize for

wide refocusing of research into Alzheimer's disease.

The two awards were made at the American Academy of Neurology's annual meeting in late April. ■

Schlessinger Will Head Society

David Schlessinger, Ph.D., has been named president-elect of the American Society for Microbiology (ASM), effective July 1, 1993.

Schlessinger, professor of molecular microbiology and genetics and director of the Human Genome Center at the School of Medicine, will become president of the society on July 1, 1994.

The ASM, with nearly 40,000 members, is one of the nation's largest scientific professional societies. Schlessinger and the other officers of the ASM oversee the society's long-range planning, publications, public affairs and educational programs.

A geneticist, Schlessinger ran for election on a platform that emphasizes the promotion of more genome work in microbiology. Microbiology helped spawn the era of modern genetics, and Schlessinger believes that genome-based approaches will have an increasing impact on biotechnology, bioremediation and infectious disease research. ■

Marker For Survival Found In Brain Cancer Patients

Researchers have found a marker for high survival rate among patients with neuroblastoma, one of the most common malignant childhood tumors.

They report that tumors with high levels of expression of the nerve growth factor receptor, TRK (pronounced "track"), show a very favorable outcome. "This finding is important because it provides a marker for good and bad prognostic groups," says Garrett M. Brodeur, M.D., associate professor of pediatrics and of genetics.

The group studied tumor samples taken from 77 patients. Each sample was examined for the presence and amount of TRK receptor and was then correlated with five-year survival rate. Eighty-six percent of patients with high levels of TRK expression had a high survival rate.

Nerve growth factor (NGF) is a protein that promotes survival and differentiation of specific nerve cells. Developing nervous-system cells that give rise to neuroblastoma have a choice of three fates: 1) continue to grow, 2) differentiate into mature cells and stop dividing, or 3) undergo programmed cell death. It appears that TRK coaxes the cells to choose differentiation or programmed cell

death, abandoning the cancerous option, Brodeur says.

Eight years ago, Brodeur's group found N-myc, a marker for low survival rate in neuroblastoma patients. The short-term impact of these studies is that the two markers can give a better idea of a patient's prognosis. "And it also gives us a way to individualize therapy and decide who

should be treated with a more aggressive drug regimen," Brodeur says. Patients with higher TRK expression and low N-myc expression might be weaned off chemotherapy earlier, he adds. Brodeur is hopeful that a diagnostic test for TRK will be available to all neuroblastoma patients in the near future.

The long-term importance of these findings is yet to be determined, but Brodeur believes they could lead to drug therapy that is less toxic than current therapy. ■

Kahn Named Director Of Medical Informatics

Michael G. Kahn, M.D., Ph.D., assistant professor of medicine, has been named director of the division of medical informatics at the School of Medicine. The appointment was announced by John P. Atkinson, M.D., professor and chairman of the Department of Internal Medicine and professor of molecular microbiology.

Kahn's research focuses on developing ways to use computerized biomedical information to solve problems in medical research and patient care. Current projects use computer databases for clinical decision support in quality assurance and infection control. He also holds teaching responsibilities for the Training Program in Medical Informatics, gradu-



Michael G. Kahn, M.D., Ph.D.

ates of which receive either an M.S. or a Ph.D. in computer science or a related discipline. The program is administered from the Institute for Biomedical Computing, a joint department of the School of Medicine and the School of Engineering. ■

BRIDGING THE GAP

Combining Neurology

And Surgery To

Transplant Nerves Successfully

by Robert Lowes

Plastic surgeon Susan E. Mackinnon, M.D., has the nerve to make basic medical research count in the lives of her patients. That's why a teenager named Matthew is walking on his own two feet these days.

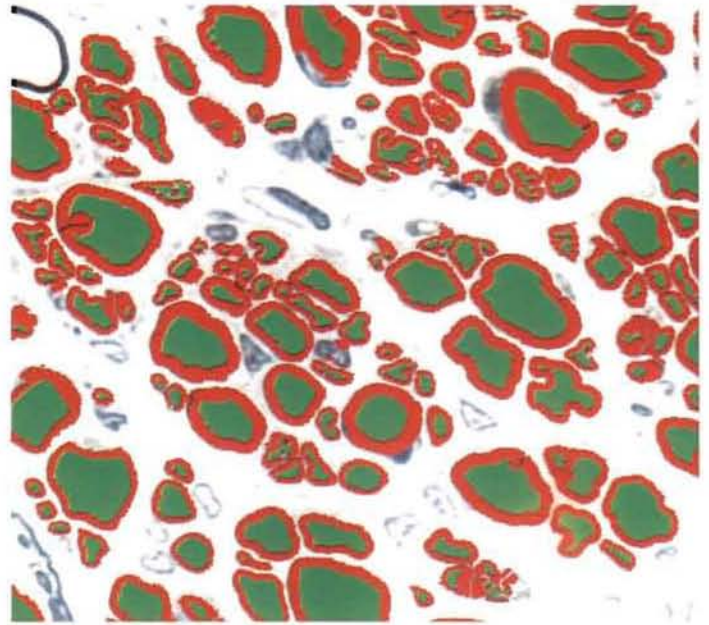
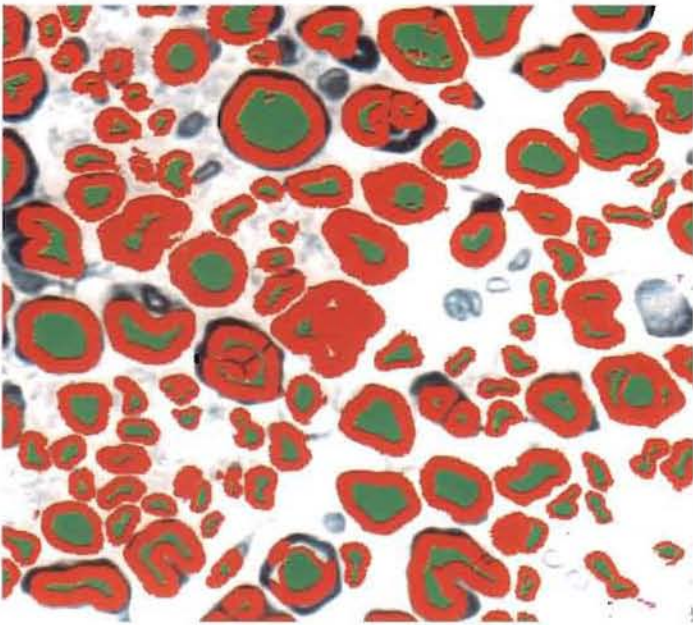
Five years ago, Matthew fell off a motor boat, and propeller blades struck his legs. Because the resulting nerve damage appeared irreparable, amputation of his left foot seemed inevitable. His plight illustrated the then-current limits of reconstructive surgery. But having plumbed the mysteries of nerve regeneration and immunology in the lab for more than a decade, Mackinnon, a professor of surgery, was able to rewrite conventional wisdom with a scalpel.

She convinced Matthew's body to accept a nerve graft from someone else without a need for lifelong dependence on problematic immunosuppressive drugs. The implications of this surgery, together with the development of nerve banks, promise to eliminate the need for patients like Matthew to rely on nerve grafts from their own bodies — or to go without one, period. "All of my research," says the Canadian-born Mackinnon, "led up to this case."

The particulars of the case were not pretty. The propeller blades had mangled the sciatic nerve in Matthew's left leg, severing it at one point. The sciatic nerve is a neural interstate highway, running from the base of the spinal cord and dividing at the thigh into the peroneal and posterior tibial nerves, the latter extending to the big toe. All of these nerves are classified as peripheral because they emanate from the spinal cord.

Besides preventing Matthew from moving his ankle and toes, his injured sciatic nerve left him with no sensation in his foot. He wouldn't be able to feel any bodily slights there — like a pebble in his shoe. This predicament leads to chronic ulceration, infection and, usually, amputation.

The nerve damage was too extensive for Mackinnon merely to stitch the two severed nerve ends together. She needed, in fact, a 23-centimeter length of healthy nerve to serve as a graft. Mackinnon had performed hundreds of nerve grafts before. But the nerve



Pseudo-color images show the results of compression injury. On the left, the two components of nerve fibers appear in a normal ratio of axon (green) to myelin (red). As a result of a compression injury (right), the ratio of axon to myelin is higher. The reduced proportion of myelin slows the travel of information along the nerve.

sections, typically five to 10 centimeters long, had been autografts — that is, they had come from elsewhere in the patient's body. Such procedures unfortunately mean double surgery and rob the patient of sensation where the graft is harvested, but they succeed.

Matthew, however, didn't have such a long section of nerve that he could afford to give up. So why not transplant a length of nerve from a donor — an allograft — as is done with hearts and kidneys? Surgeons have tried doing it with nerves since 1878. And they've had plenty of incentive. Allografts eliminate the injury and scarring that attends the harvesting of tissue from the patient's body. Plus, they give surgeons greater variety in the nerve tissue available for transplant.

But until 1988, nerve allografts had been confined largely to the realm of wishful thinking. Published research cast serious doubt on the possibility of bringing severed nerves back to life. After all, the body's immune system persecutes such foreign tissue.

To be sure, transplant specialists possess a remarkable drug, cyclosporine, that suppresses the immune system and prevents rejection. But the drug, normally taken for the rest of a transplant patient's life, can produce serious side

effects including kidney and liver damage, hypertension and depression.

"We can't sign up patients for this type of immunosuppressive toxicity if we're not saving their lives," says Mackinnon. Transplants of nerve allografts to restore the use of a foot have not warranted a lifetime prescrip-

tion of the drug. So, according to conventional wisdom, Matthew had only a likely amputation to look forward to.

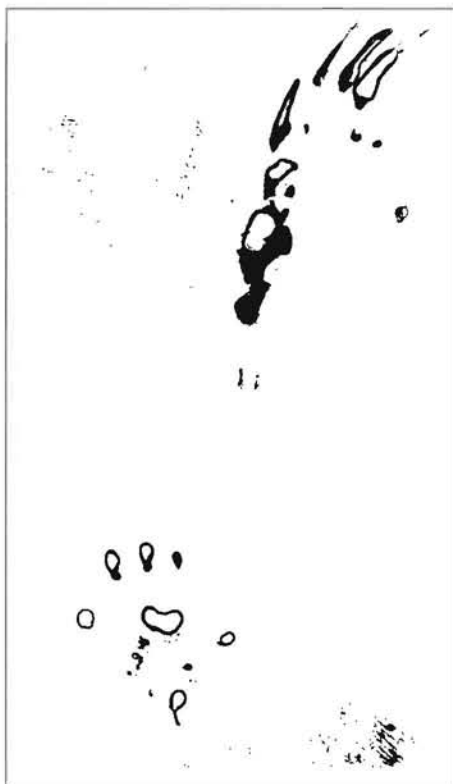
Mackinnon, however, had been conducting research to realign conventional wisdom. A nerve allograft, she hypothesized, might be successful with only a temporary regimen of cyclosporine. Mackinnon launched her investigation while on the faculty at the University of Toronto and continues it here.

The human nervous system is fascinating partly because of its complexity. When a nerve is cut, it's like snipping a cable to find that it is composed of many smaller wires. Each one of those is a bundle of even smaller wires. The nerve bundles are called fascicles. The neural wires inside fascicles are axons — the essential nerve tissue that transmits signals to and from the brain. Axons relaying vibration and movement signals are sheathed with myelin, a protective tissue made by so-called Schwann cells, Mackinnon explains. Axons for pain and temperature are unmyelinated. Besides producing myelin, Schwann cells string together to form a kind of tubing that encloses or supports the axon.

An individual axon is not a distinct entity but instead the long arm of a



Plastic surgeon Susan E. Mackinnon, M.D., practices peripheral nerve surgery at Barnes and St. Louis Children's hospitals.



To assess functional recovery after nerve injury, Mackinnon and her colleagues dip the feet of laboratory animals in developer, then walk the animals on X-ray film to record their tracks. Here, a rat's left hind foot is normal; the right side displays nerve damage evidenced by the long track and relatively short toe spread.



Research assistant Daniel Hunter uses the digital image analyzer to assess a histologic slide of peripheral nerve.

nerve cell that extends from the cell body. An axon that reports a prick in your big toe is part of a cell that has snaked its way there from the spinal cord. If its cell body were the size of an average person, the axon would stretch for eight miles.

Cell bodies of nerves that wire the body for voluntary and involuntary movement are nestled in the so-called anterior horn of the spinal cord. Their axons sprout delicate endings that form synapses with muscle tissue. Cell bodies of sensory nerves lie in nerve tissue just outside the spinal cord; their axons terminate as free nerve endings or specialized receptors, like those for touch.

When an axon is severed, the segment closest, or proximal, to the spinal cord will grow unmyelinated feelers that seek the outlying, or distal, segment, says Mackinnon. At the same time, Schwann cells in the distal segment proliferate. They give the axon a structure to advance along at the rate of about one inch per month, and they produce chemical factors that encourage the axon to move forward. Schwann cells also wrap the axon with myelin if the axon was originally myelinated. The regenerating axon doesn't stop growing until it reaches the appropriate muscle tissue or sensory outpost.

Surgeons turn to grafts when the gap in a severed nerve is too long for the axons to span. Essentially, a nerve graft provides the vine-like axons with new Schwann cells that serve as a neural trellis. All of this basic neurology came into play when Mackinnon and her colleagues began investigating allografts and immunosuppression.

In one study, pieces of sciatic nerve were grafted into the hind legs of 14 laboratory rats. The



The glass knives used to section nerves for study via light and electron microscopy.

animals received cyclosporine for eight weeks to disarm their immune systems. The rats on cyclosporine gained increasing function in their hind legs for eight weeks and then slipped in motor performance over the next six weeks. The reason? The immune system, no longer suppressed, was attacking the nerve graft and its Schwann cells in particular. There also was microscopic evidence of rejection — at 14 weeks regenerating axons had unusually thin layers of the myelin made by the hard-pressed donor Schwann cells.

This rejection of the nerve grafts, however, was short-lived. After week 14 of the study, the rats' motor recovery was on the upswing. And at 20 weeks, the myelin surrounding the axons had thickened considerably. The repaired nerves were thriving again, says Mackinnon, because the rats' own Schwann cells — safe from the immune system's hostility — were repopulating the grafts and fostering axonal regeneration. Only a short course of low-dose immunosuppression is required for results that equal an autograft.

Mackinnon has since replicated these findings on temporary immunosuppression and rejection in a larger study involving 150 animals studied over 30 weeks. However, she had enough evidence in hand in September 1988 to justify experimental surgery when Matthew was referred to her for a nerve transplant. Several days later, St.



Nerves are embedded in epoxy resin prior to sectioning.

Michael's Hospital in Toronto found a suitable donor — a 15-year-old girl killed in an auto accident

"At the time, I was in Ottawa to receive an award from the Royal College of Physicians and Surgeons of Canada for my research," says Mackinnon. "There I was dressed and ready to go to a black-tie dinner. I caught the first plane to Toronto. It was all very rushed."

The surgery succeeded, but Matthew has not regained motor function in his left foot. That's predictable, says Mackinnon. "Sensory receptors will wait pretty much forever to be reinnervated, but muscles are under a time clock. We have to reinnervate them before a particular time, or they won't work." Still, Matthew can move his left leg well enough to walk. Most importantly, his left foot can feel a pebble, a bee sting or a tuft of grass, even though cyclosporine treatments stopped in 1990.

"He thinks it's pretty much like his normal foot, although he does wear an ankle brace and limps a little," says Mackinnon. "He rides his bike, plays baseball and walks barefoot on the beach. He's as happy as he can be."

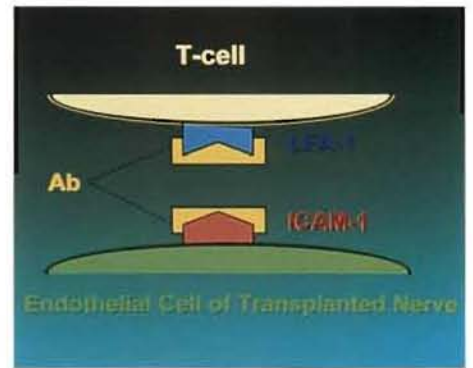
Mackinnon hopes to capitalize on the feasibility of nerve allografts by developing nerve banks for their storage. She and her research fellows in Canada have found that animal nerve grafts refrigerated for up to three weeks work as well as fresh grafts. Plus, chilling the donor

tissue appears to cool the body's immunological ire. The laboratory here continues to work on the many aspects of nerve allografts — from regulating the immune response to methods for storing nerves as transplant material.

In Matthew's case, when a donor graft became available, Mackinnon had to operate immediately. A nerve bank would eliminate the haste. "We will have more time to get a better histocompatibility match between donor and patient. We can test for viruses in the graft in a more controlled fashion. The nerve bank lets us make transplantation an elective procedure instead of an emergency procedure, which will lower the cost," Mackinnon says. "Many patients will benefit from this. It may take 10 years to get a nerve bank going, but we will."

Mackinnon the surgeon operates on approximately 400 patients a year, all of them with damaged peripheral nerves. Her patient Matthew remains the world's only successful recipient of a nerve allograft. To Mackinnon, situations like his demand more communication between neurological researchers and surgeons, both of whom occasionally have functioned like loose ends of a severed nerve. "Peripheral nerve surgery is being done by plastic surgeons, orthopedic surgeons, neurosurgeons, general surgeons, you name it. It fits into so many specialties that it hasn't developed a niche yet," she says. "Patients with these injuries are sometimes being treated haphazardly."

The unifying element will be the neuroscience, Mackinnon believes: "Neuroscientists are among the purest of the basic scientists. They have a lot of information we



Work by Yasushi Nakao, M.D., Ph. D., and Catherine Gilliam, M.D., in Mackinnon's laboratory concentrates on using antibodies to prevent the immune system from attacking a transplanted nerve. When highly specific T-cell receptors are blocked by the antibodies, a nerve graft is accepted without systemic side effects.

surgeons can extrapolate for our patients with cut-up nerves — if we can speak their language, if we can get into their literature. I want to be a liaison between the two groups."

Or a graft, if you will, of medical ingenuity. ■



Doug Ball (foreground), a student in the M.D./M.A. program, and Catherine Gilliam, M.D (background), a resident in plastic surgery, conduct research in Mackinnon's lab. Ball studies the effect of age on peripheral nerve regeneration. Gilliam works on a variety of projects in the hope of establishing a nerve bank for future human transplantation.

More Than Meets

As you read these words, your brain performs a task that today's best supercomputers can't equal. And you don't even realize it is happening. The wiring, circuits and switches that crisscross your brain underlie an information network that takes in visual information and makes sense of it without your having to think about it.

by Jim Keeley

The Eye

Learning How We See

Scientists delving into the process of how we see have learned that there's more to vision than meets the eye. So much information floods our eyes that the retinal ganglion cells — the cells at the back of the eye that transmit electrical signals to the brain — prune away nearly 99 percent of it before the brain even begins to process the image. Nearly 99 percent of the information is lost and still we can see. How is that possible?

This is the sort of question that gets the attention of David C. Van Essen, Ph.D. His appointment as Edison Professor of Neurobiology and head of the Department of Anatomy and Neurobiology has thrust the School of Medicine into the middle of one of the hottest debates in neuroscience: How does the human brain process and make sense of visual information?

Van Essen suspects that the brain is more complex than the most powerful computer humans are capable of developing. But, provocatively, he believes that man-made computers may be the key to deciphering the complicated information networks that distinguish the human brain. Computational neuroscience, as this branch of science is called, is a relatively new field that combines researchers' ideas and



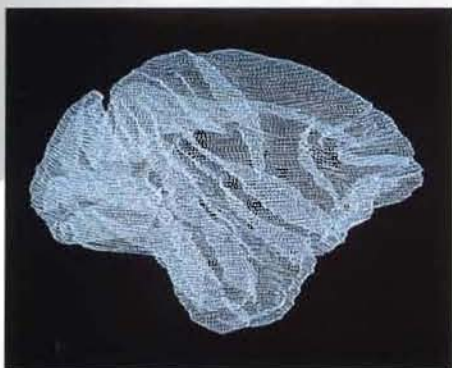
David C. Van Essen, Ph.D., views a large, physical model of a macaque's brain, with the areas dedicated to visual processing highlighted in various colors.

intuition with experimental evidence and computer power to crack the code of the ultimate computer, the human brain. Van Essen is one of the field's founders.

Seeing and Recognizing

Dwelling on the few milliseconds that occur between seeing and recognizing is not easy, but Van Essen has learned from the best. As a postdoctoral fellow in the Harvard University laboratory of David Hubel and Torsten Wiesel, Van Essen helped two future Nobelists open a new window on the brain. "They showed that one could glean remarkable insights about the properties of individual nerve cells and how those cells respond to visual stimuli," Van Essen says. "It was tremendously exciting in the 1960s and 1970s to finally understand some of the initial stages of processing in the visual cortex."

Hubel and Wiesel won a Nobel Prize in Medicine or Physiology in 1981 for demonstrating that cells in the visual cortex respond selectively to stimuli, such as bars, edges of light and direction of motion. They showed the brain at work, analyzing minute regions of the visual world for characteristics (such as shape, contour, motion and orientation) and assembling that information into a coherent picture — the process we call seeing.



Three computer-generated reconstructions of the macaque brain. On the left, 85 two-dimensional contours have been stacked and connected by computer into 120,000 triangles. In the center, the triangles have been filled in to form a continuous surface, thereby providing a view down into the folds, or sulci. The reconstruction is by assistant research scientist Heather Drury, M.S. On the right, the computer has recorded the positions of cells labeled by a tracer injected into a distant area of the brain. The labeled cells are displayed in a three-dimensional reconstruction of the cerebral cortex's gray matter.

From that work, scientists subsequently showed that visual processing is the product of a series of lightning-fast steps that take place in distinct areas of the brain. Neurons receive the initial signals and respond to simple patterns, such as arrays of light and dark bars. As raw information about what the eyes are focused on moves through successive levels in the brain, specialized cells filter the information. At the final stages, all of that information is meshed together, and we recognize an object. Though Hubel and Wiesel provided a fresh

perspective on the initial stages of visual processing, researchers remained largely in the dark about how cells that respond to specific stimuli work together to process complex images and form a smooth, unbroken picture of the world.

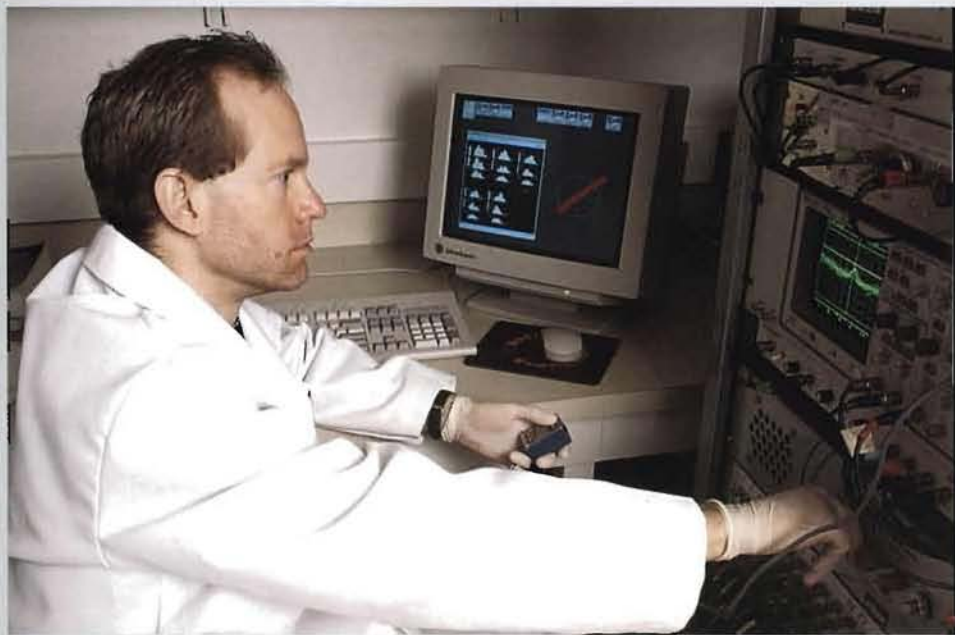
That was the problem Van Essen wanted to solve. Instead of focusing on the primary visual cortex, he concentrated on higher levels of the brain — areas where complex images are decoded and recognized. The techniques that Hubel, Wiesel and others had developed for exploring the visual brain

were important, but it became clear to Van Essen and others in the 1970s that if they were to see how the brain organizes the flow of information and forms an unbroken picture, new tools would be required.

And computational neuroscience was born. Before there was such a field, there was a group of scientists who felt that the lack of strong mathematical formulations and models was a great barrier to understanding visual processing. Fortuitously, just as this field of neuroscience was beginning to take shape, the computer revolution was occurring. Van Essen and others began to view the computer as a valuable ally. Today, the computational group is still a minority of neuroscientists, but their theories and data are rapidly overturning long-held notions about the brain. For example, the theory that the brain is neatly partitioned — one area for color vision, one area for depth perception — is giving way to a more flexible description that says these different functions may be intertwined.

Interconnections

Van Essen's several research projects may seem discrete to the outsider, but they are richly interconnected. In that sense, they mirror the organ he is studying. The three categories of projects — anatomical, physiological, and computer modeling — are all designed to extract information about



Ed Connor, Ph.D., a postdoctoral fellow, tests the responses of individual neurons to a variety of visual stimuli as the animal attends to different locations on a computer screen.

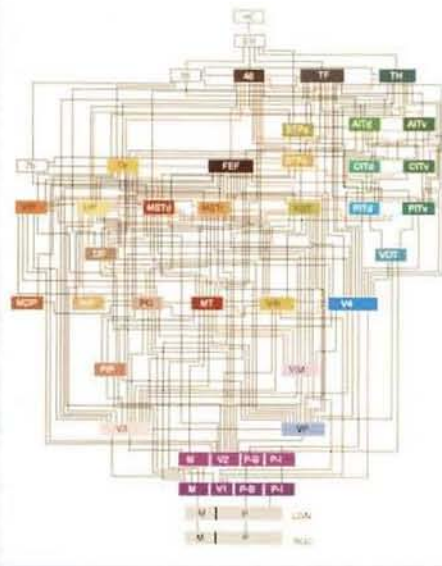
the visual system. Experimental work uses macaque monkeys. Although it is 10 times smaller than a human brain, the macaque's brain nonetheless displays a striking similarity to a human's.

At the turn of the century, classical anatomists had identified three distinct areas in the brain responsible for visual processing. This model persisted until well into the second half of this century. In 1979, Van Essen wrote a review article describing visual areas in the cerebral cortex — only six had been identified at the time. "It wasn't really until the 1980s that there was an explosion in the number of identified areas," Van Essen says. A current tally shows a mind-boggling 32 distinct but interconnected areas in the macaque brain responsible for interpreting and assembling the macaque's visual world.

Having to keep track of detailed experimental data on each of the 32 areas is overwhelming, Van Essen says. Scientists now believe there may be as many as 40 visual areas in the macaque brain, and Van Essen hopes there aren't many more. One goal of his work is to identify all of them. As each visual hotspot is isolated, researchers tease out the neuronal wiring that connects one area to another. Knowing where the visual areas are and how they communicate provides a source of information for the group's attempts to build a computer model of visual attention.

Charles H. Anderson, Ph.D., research professor of neurobiology, and predoctoral student Bruno Olshausen are developing a computer model that replicates as many of the human visual processing system's functions as possible. They have successfully taught a computer to discriminate and recognize a specific letter from a field of letters surrounding it. Faithful to the brain's actual method of operation, the system tests theories of visual attention.

Anatomical data also feed the voracious appetites of various national and international brain-mapping projects that are hungry for more detail. Lately, neuroscientists have promoted building a computerized brain map database. The computational nature of Van Essen's work makes him a logical apostle of the



Van Essen and his colleagues have summarized what is known about the 305 pathways that interconnect the 32 distinct cortical areas of the macaque brain associated with visual processing. This "wiring diagram" depicts the hierarchy of the visual areas and their interconnections. (Reproduced with permission, from *Science*, "Information Processing in the Primate Visual System: An Integrated Systems Perspective," Vol. 255, page 421, January 24, 1992, © AAAS.)

brain-mapping initiative. And, in fact, he has been working on several parallel projects that will make data on the visual system more manageable and accessible.

The first is a graphical database that will allow scientists and students to ask better questions about the visual system more effectively and more efficiently. Such an on-line brain map would hold the latest information about any area of the visual brain. A researcher wanting the current thinking about the pulvinar nucleus, a small structure that some scientists believe is the "consciousness command post," could click his computer's mouse on the pulvinar nucleus and a torrent of information, from journal articles to experimental protocols, would become available. Van Essen's team also is assembling a detailed map of the macaque brain on high-resolution graphic computers.

Computers might help resolve another issue confronting neuroscientists. Insights gleaned from studying the macaque visual cortex have been relevant to what goes on in the human brain, Van Essen says, but there has been difficulty in precisely comparing functions in the two brains. Though the human brain is 10 times larger than the macaque's, researchers can't make a direct comparison simply by enlarging a monkey brain to the size of a human brain, Van Essen notes. Part of the solution may come from his collaboration with Michael Miller, professor of electrical engineering, to use "warping algorithms," sophisticated computer programs that allow one brain to be warped into the shape of another. Warping algorithms also will be valuable for physicians comparing the brain of an ill patient to that of a normal person, since no two human brains are identical.

It is only fitting that in Van Essen's lab much energy is devoted to understanding the behavior of small groups of neurons in the visual system, à la Hubel and Wiesel. These investigations — Van Essen labels them "physiological studies" — allow scientists to discern the idiosyncrasies of small populations of neurons within a larger visual area.

Many different patterns have been used to probe the visual system. The premise is that if you find the right stimulus and present it to a monkey during testing, the neurons that respond selectively to that visual stimulus will sing out. The goal is to explore responses to different stimuli. If researchers use patterns that are too complex, such as a picture of a face or a hand, cells may respond, but there is no way to interpret accurately what component of the image those neurons are responding to.

In fact, a subset of cells in the temporal lobe responds to complex hand and face patterns. "That tells you that you are probably on the right track for finding cells involved in complex pattern recognition. But the question of how those cells attain their properties is very difficult to decipher. You can't take something like the face and break it into

its component parts and systematically evaluate the relative contributions of those parts in a well-controlled way.”

Recent work by Van Essen and postdoctoral fellow Jack Gallant, Ph.D., hints at the existence of a group of cells that may serve an intermediate role in the recognition of complex patterns. Sticking with the dictum that the best stimuli to use are well-defined mathematical shapes, Gallant convinced Van Essen to try an experiment using concentric rings and spiral shapes as stimuli. Initially skeptical that such studies would prove fruitful, Van Essen gives Gallant much of the credit for their findings.

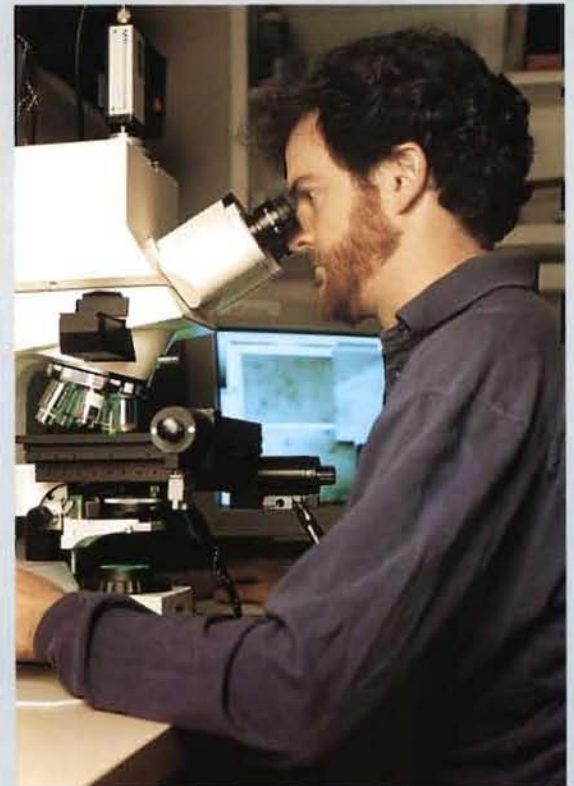
The work, which recently appeared in the journal *Science*, shows that cells in area V4 of the brain show a striking degree of responsiveness to concentric rings or spiral shapes. Van Essen is fascinated by the finding because it may offer a lead to reaching his elusive goal of understanding how complex images are recognized. “Our hypothesis is that these cells are an intermediate stage on the way to more complex pattern recognition,” Van Essen says.

At the intuitive level, this thinking makes sense, he notes, because in the natural world there are many structures, like flowers, that are dominated by

concentric patterns. Concentricity may be one of the necessary and proper stimuli that neurons in V4 respond to in order for higher level brain structures to recognize a flower. The group plans to explore further classes of stimuli that they think also may contribute to subsequent stages of visual processing.

Although this branch of neuroscience is extremely young, Van Essen hopes that the ideas will one day move out of the lab and into everyday use. Understanding the brain and its visual system from many different perspectives may have enormous benefits. One example: The wide-angle approach Van Essen and his colleagues take may turn up general organizing principles that are at work throughout the brain. “We study the visual cortex not simply for a fascination with vision, but with the realization that it is an excellent model for the organization and function of the entire cerebral cortex,” Van Essen says.

Many maladies attack the computer within – strokes, tumors, epilepsy and psychiatric disorders among them. But



Postdoctoral fellow Tom Coogan, Ph.D., collects data from brain sections with a computer-driven microscope.

the complexity of the system may be our saving grace. The work of Van Essen and others challenges the long-held notion that the brain compartmentalizes its functions, one function per area, like today’s computer systems. The evolving principle is that, instead, many functions are intertwined to create a fast, faithful and flexible system. As Van Essen says: “The relationship between functions and partitions in the brain is complicated, because the system has a distributed workload. All regions of the brain are specialized to some degree, but they are not overspecialized.” Developed with these organizing principles in mind, the computers of tomorrow may edge closer to the powers of the brain. ■



“Polar gratings” are used by postdoctoral fellow Jack Gallant, Ph.D., to test the responses of single neurons in an area of the macaque’s brain dedicated to visual information processing. The response of the single neuron represented here ranges from none (dark blue) to vigorous (red). The cell being tested was highly selective for a restricted group of similar patterns.

ONWARD

The National Council Collaborates To Map The Medical School's Course

by Steve Kohler

I ncreasingly, medical science's advances are the result of interdisciplinary collaboration. The complexity of the issues addressed by modern medicine demands that microbiologists, immunologists, radiologists, surgeons — scientists and clinicians of every stripe — work together to blend expertise, approach and experience. The issues confronted by medical school administrators are no less convoluted and thorny.

William A. Peck, M.D., executive vice chancellor and dean of the School of Medicine, has tapped the school's long history of productive collaboration to assist him in steering the institution through waters that get choppy as the wind level surrounding healthcare, research and educational issues rises.

The medical school's National Council was formed three years ago to "advise and counsel," in Peck's words. An august body of 24 prominent men and women from a broad assortment of endeavors, the council now meets twice each year to consider the medical school's direction. Indeed, the university's overview of the National Councils says, "The purpose of the Councils is to monitor, offer advice, assistance and criticism to the dean and other administrative officers...."

The councils were established by the Board of Trustees in May of 1986 as a result of the recommendations of the Commission on the Future of Washington University. Currently, there are nine National Councils: Seven serve schools of the university; one offers advice concerning Olin Library, and one advises on the issues of student affairs.

The medical school's National Council looks at the biggest picture: the goals and missions, plans and processes of the medical school, not the details of curriculum or budget that many other visiting committees address, Peck explains. "The National Council has allowed me access to individuals who are highly intelligent, experienced and wise, as well as being enthusiastic about our institution," Peck says. "Among our members are those who are knowledgeable about all medical schools, not just this one, and people with an awareness of the community from both a regional and national perspective. And I haven't been

disappointed; the group has more than fulfilled my expectations," he says.

Much of the responsibility for the group's efficacy, according to Peck, lies with its chairman, Robert J. Glaser, M.D. "Few people are as knowledgeable about medical schools and academic medicine," Peck says. Glaser, who was on the Barnes Hospital house

Glaser points out that the council is "not a governing board; we have no veto power. But it brings together interested and knowledgeable people from many facets of society to advise the administration. Some are business leaders, others are active in healthcare, and several are well-known academicians. This multidisciplinary approach

lets each of us focus on the details about which he or she knows something."

Glaser applauds the medical school for its active role in "confronting the complex healthcare issues that involve our society."

National Council member Raymond H. Wittcoff says the issues under consideration are very complex. A university trustee, past chairman of the board of Jewish Hospital and of the Medical Center, a successful developer of major office buildings and a director of the Equitable Life Assurance Society, Wittcoff says that in a comparison between the Medical Center and the corporate world he inhabits so successfully, he finds the business world relaxing.

"We live in a time when there's much discussion about what's wrong with America, and we do have to make some fundamental changes," Wittcoff says. "But the success of our great research institutions and this medical school in particular is gratifying. Their preeminence is indisputable. We are not lagging behind any other nation."

Council member I. Jerome Flance, M.D., a 1935 graduate of the School of Medicine, a professor of clinical medicine and the recipient of the Alumni/Faculty Award and the university's Founders Day Award, sees his role on the council as that of friend. "Our role is as a sounding board," Flance says. "We don't consent or



Robert J. Glaser, M.D., chairman of the National Council, engages in discussion with William A. Peck, M.D., executive vice chancellor and dean of the School of Medicine.



National Council member Charles F. Knight makes a point about the medical school's future as part of a full-service healthcare system. Also pictured is Raymond H. Wittcoff.

staff and began his academic career here, has been dean of Colorado and Stanford medical schools and acting president of Stanford. He has served as a trustee of Washington University since 1979 and has held executive positions in three major, medically oriented foundations for a total of almost 25 years.

dissent, we counsel. We are friends, there to offer constructive help, though if we saw something terribly wrong going on we would say so. But that's not the case now."

Although Peck consults with individual council members regularly and carefully heeds the council's advice, much of the information during the first five meetings flowed from administrators and key faculty to council members, according to Glenda Wiman, assistant dean for special programs and the person responsible for arranging the meetings. However, at the most recent meeting, held in early May, councilors more actively discussed issues faced by the medical school.

In the early meetings, the council learned about and visited each of the affiliated hospitals, heard presentations about major research and construction projects either underway or planned and was brought up to date concerning medical school and Medical Center history.

At meeting number six, attention turned to the clinical future of the institution and the serious issues facing all healthcare entities. Peck told the group about developments at the medical school and its affiliated hospitals, then presented his administration's vision of the post-healthcare reform future. He spoke of coming problems for funding academic health centers, of increased competition for market share, of the impending dominance of managed care (represented by the health maintenance organization, or HMO) and of the inevitability of competition between providers being managed by a governmental agency, either state or federal.

Most importantly, Peck detailed the opportunity facing the Medical Center to direct its own evolution into a top-

quality, integrated healthcare system that offers a full range of services and a competitive price. Such a full-service system will offer everything from ambulatory and home-based care to the kind of tertiary and quaternary care provided by the super-specialists of the School of Medicine.

Commenting on Peck's presentation,

Barnes, Jewish, Inc. (BJI), pointing out that in order to be successful, any such system must be seamless, without a gap in its abilities. Glaser observed that ridding the current healthcare system of its duplication of services — all deeply ingrained — will be among the sticking points to reaching a new, more efficient form of national healthcare.

The challenge Wittcoff sees is for the medical school to maintain its character as a great research institution while taking on an expanding clinical responsibility. "I'm confident it can be done," he said. "There need be no conflict between cost control and quality control. The same leadership that controls costs may be the kind that promotes quality. I am more optimistic right now than at any other time during the 25 years I've been watching these institutions." Both Wittcoff and Glaser express great admiration for Peck's leadership skills and for his ability to handle effectively the burdens of his office.

Peck returns the compliment: "The National Council members have been a tremendous asset for me as a leader, and it would be hard to replicate their assistance in any other way." Council members Knight and John P. Dubinsky, in fact, have been instrumental in realizing BJI and in bringing about the affiliation of the Christian hospitals.

With Peck steering and the council members advising and watching for obstacles, the hope and the plan is that the School of Medicine will be transformed and brought smoothly through the rough passage ahead. On the other side lies continued preeminence as a research institution based on broader support from greatly expanded clinical activities. ■

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Wittcoff called the opportunity "awe-inspiring." He said, "We're moving into an arrangement that I didn't expect until the next century." Lengthy and candid discussion followed, with council member Charles F. Knight, chairman of the board and CEO of Emerson Electric Co., chairman of the board of Barnes Hospital and of

BREAKING THE SILENCE

A Rare And Deadly Cancer Gives Up Its Secrets

Sandra Gray cries every time she talks about her father and brother. Seventeen years have elapsed since their deaths, but time hasn't dulled the pain of their passing. Nor has it erased from the family's bloodline the rare illness that claimed them and continues to stalk the St. Louis woman, her children and other members of her family.

BY KLEILA CARLSON

The disease, multiple endocrine neoplasia type 2, or MEN 2, can traverse generations, quietly passing from parent to child. The genetic illness, which causes a specific cluster of diseases, has been traced to Gray's father's family.

Sandra Gray and her daughter Gia, along with other members of the family, have battled MEN 2A, a rare but virulent form of cancer. Gia still wears a bandage after her recent thyroidectomy.



Like her father and brother, Gray carries the gene for a specific type of the disease known as MEN 2A, a disorder that can cause medullary thyroid cancer, pheochromocytomas (or tumors of the adrenal gland) and hyperparathyroidism in people between the ages of five and 45 years.

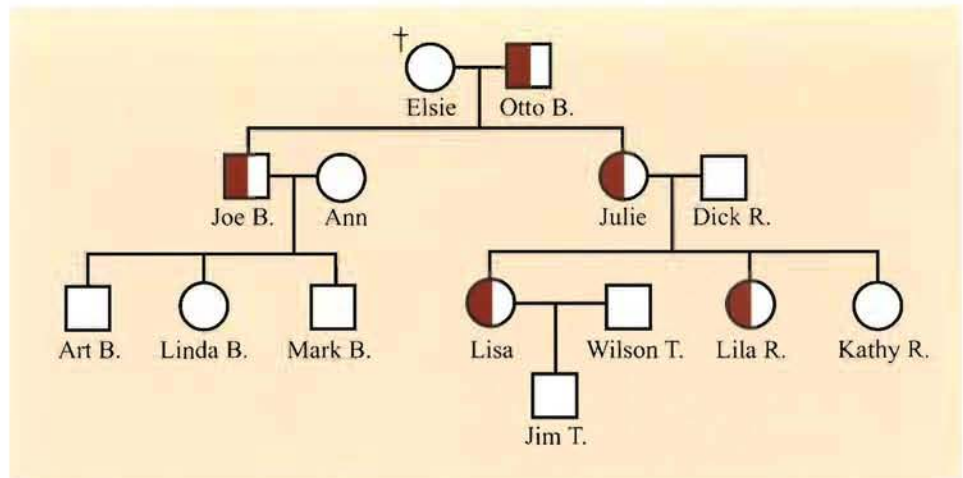
Gray's father and brother had both medullary thyroid cancer and pheochromocytomas, which about one-third of MEN 2A sufferers develop. After their deaths, extensive tests were run on Gray, her siblings and others from her father's family. Gray, who was found to have a pea-sized tumor on her thyroid, had the gland removed in 1977; tumors also were discovered in her younger brother and half-sister by her father's previous marriage. Since that time, a nephew, several aunts, uncles and many cousins also have had tumors removed.

Gray is still tested yearly for the development of pheochromocytomas, which can cause hypertension and sudden death, but she is most concerned for her children. In May, her youngest daughter, Gia, 19, was found to have a tumor on her thyroid. The gland was removed at Barnes Hospital in June. So far, Gray's three other children, who range in age from 17 to 25, have been disease-free. "Every time the kids get sick, I watch for symptoms (of MEN 2A)," says Gray. "I get very detailed about asking them how they're feeling. Even though all of them have been tested since they were small, I was stunned when they told us Gia needed surgery.

"When you're not in pain, it's hard to believe there's something wrong with you. The scary thing about medullary thyroid cancer is its silence — you may not know you have it until it's too late."

SPEAKING OUT

Attempting to better understand the disease is Samuel A. Wells Jr., M.D., Bixby Professor of Surgery and chairman of the Department of Surgery, who has spent a quarter century tracking this quiet killer that strikes its victims in their prime. Wells and his research group test and monitor about 2,000 people in 48 states and several foreign



A family pedigree traces the path of MEN 2A. Darkened figures indicate disease gene carriers. This pedigree presents a classic example of the transmission of a dominant disease gene.

countries with four different hereditary endocrinopathies: MEN 1, MEN 2A, MEN 2B and familial medullary thyroid carcinoma (FMTC).

One of a handful of physicians and scientists worldwide studying MEN 2A and its associated syndromes, Wells became interested in the malady about 20 years ago when, as a surgeon at the National Cancer Institute in Bethesda, he cared for several patients with the disease. Over the last several years, the group of investigators working on the MEN problem has expanded to include pediatricians, pathologists, molecular biologists, geneticists, biostatisticians and social workers.

"The ultimate goal is to perform a thyroidectomy on these children before they develop medullary carcinoma," says Wells. "Removal of the thyroid is generally well tolerated by children."

Because MEN 2A is caused by a dominant gene, only one copy of the defective gene must pass from parent to child for the disease to develop. That means anyone with an affected parent has a 50 percent chance of developing the disease. Patients with MEN 2B develop medullary thyroid carcinoma and pheochromocytomas. They also have a typical physical appearance so that they are easily recognizable on sight. Patients with MEN 2B have a very aggressive form of medullary thyroid carcinoma, and they often succumb to the disease at a young age. Patients with FMTC only develop medullary thyroid carcinoma. Unlike MEN 2B, patients

with FMTC have a relatively mild form of medullary thyroid cancer. In screening these families, every effort is made to diagnose the medullary cancer as early as possible, since patients can often be cured if the tumor is confined to the neck at the time of operation.

Helen Donis-Keller, Ph.D., director of the division of human molecular genetics in the Department of Surgery, led an effort to identify the gene(s) responsible for MEN type 2 syndromes. Her laboratory found mutations in the RET proto-oncogene in MEN 2A and FMTC families. The normal function of the protein coded by the RET gene is not known at this time. However, it is known that the gene is expressed early in development and is probably involved in the development of neuroendocrine cells.

The RET protein is a member of a family of membrane-spanning tyrosine kinase receptors. "We found that the DNA mutations cause changes in the protein sequence which we suspect alter the three-dimensional structure of the extracellular domain of the RET proteins," says Donis-Keller. "Since this region binds a ligand which initiates a signaling mechanism, it seems reasonable that a change in the structure could alter this process. One of the next steps is to identify the ligand and how it interacts with the RET protein so that we can begin to understand how the mutated protein causes disease."

Donis-Keller's group has also found a mutation in a sporadic case of medullary

thyroid carcinoma, leading her to believe that RET plays a more general role in the development of thyroid cancer. Although Donis-Keller expects that RET may also be responsible for MEN 2B, the most serious of the MEN disorders, genetic mutations have not yet been found.

"In the MEN 2A and FMTC families we are currently studying, we know what mutation each family carries and that everybody in the family has the same mutation," says Donis-Keller. "This allows us to do predictive diagnosis and determine with high certainty who has inherited the mutation for disease. Everyone who inherits the mutation develops disease."

Until now, the most reliable test available to determine disease was the calcium-pentagastrin stimulation test, a biochemical assay in which calcium and pentagastrin are given intravenously to stimulate the thyroid's secretion of the hormone calcitonin. Elevated levels of calcitonin are an indication for medullary thyroid cancer.

Donis-Keller says the 10-minute test is unpleasant, not as accurate as DNA testing and must be repeated annually or semi-annually. "DNA testing can be performed early in the lives of these people, and the test only has to be done once. This will relieve a lot of anxiety in people, because we can tell them whether they carry the disease gene. Those who carry the gene can have surgical treatment, because this is a completely curable disease if caught early."

ON THE TRAIL

To catch the disease in its earliest stages, the research group travels to the remotest of areas and to metropolitan regions to test patients who range in age from four years to over 90. Unlike cystic fibrosis, which is primarily restricted to Caucasians, or sickle cell anemia, which occurs only in blacks, MEN 2A does not discriminate on the basis of race. Neither is it influenced by sex or geography.

The excursions began when Wells launched his investigation into the illness with a family that came to Philadelphia from Western Europe in the 1700s and settled in the mid-Atlantic states. One of the largest families he

follows spans the country from Virginia to Alaska. Nationwide, he monitors 36 families with MEN 2A. Members of about 10 different MEN 2A families live in Missouri.

"We spend a lot of time screening family members in the field and genotyping them because they cannot come to us," says Wells. "We may screen a group of 100 people in a morning, or we may see only two. Sometimes we work in a clinic or an office and sometimes from a patient's home."

On a recent screening trip to Pennsylvania and Maryland, the living room of a patient's home was turned into an examination area for 87 family members because there was no clinical site available. On the same trip just a few hours later, families were tested in a state-of-the-art laboratory at the National Institutes of Health in Bethesda. "Other healthcare providers and hospitals have been extremely helpful in assisting us during these studies," Wells says.

"A mother, father and three children had to be screened, and they had no transportation," says Mary DeBenedetti, R.N., research nurse and patient coordinator for Wells' research project. "Sometimes, we have to accommodate the family's circumstances, and we do."

DeBenedetti, whose role is pivotal to the project, plans and coordinates every

screening trip. She is responsible for everything from calling patients to set appointment times and arrange their transportation to contacting families to log all births, deaths, divorces and disease occurrences. She also tests patients and notifies them of their results, and patients turn to her with their questions and concerns.

"This is an uncommon disease, and patients need to know they can call us if they have questions or concerns," says DeBenedetti, who spends more than 85 percent of her time on the telephone keeping tabs on the 93 families in Wells' study. "We want them to know we are concerned about their health and the health of their families."

Gray's family has taken part in Wells' study for the last five years. Before that, other St. Louis physicians annually tested her family. "I was blessed, I think," says Gray, a second-grade schoolteacher. "They caught my (thyroid) tumor early, and I didn't hesitate to have surgery."

Gray, 49, has been free of disease for 16 years. She says one benefit of participating in a nationwide research program is the education patients receive about their illness. "We are apprised of the latest research findings and developments, and we don't forget appointments because they call us and make sure we keep them. It's a very thorough and worthwhile program." ■



Mary DeBenedetti, R.N., counsels patient Becky Killian, a member of the MEN 2A study. Killian had her thyroid removed in May after a tumor was discovered.

Student Stage

Match Day 1993

Earlier this year, approximately four out of every five students participating in Match Day received a residency position at one of their top-choice institutions. Ninety-two students took part, and 82 percent (75) will be doing their postgraduate training at one of their top three choices of institutions. Fifty-six percent will train at their first choice.

Five students found positions independent of the matching program, and four graduating students decided not to take residencies immediately. For those taking part in the matching program, interest in internal medicine programs declined but remained high, while residencies in pediatrics, family practice and orthopedic surgery became more popular. In 1993, the number of new physicians choosing to pursue family practice (nine) more than doubled from last year. Internal medicine and pediatrics tied for the most frequent choice among graduates, with 17 selecting each; eight will go on in orthopedic surgery.

Forty-one of the new physicians will remain in St. Louis for their postgraduate training, 32 of them at Washington University or affiliated institutions. Other popular destinations were Boston (10), the State of California (7) and New York (5). The complete list fol-

lows. Some names may be listed more than once because of preliminary and transitional residencies.

ARKANSAS

Little Rock
Univ. of AR for Medical Sciences
Orthopedic Surgery
Gannon, Patrick R.

CALIFORNIA

Los Angeles
UCLA Medical Center
Anesthesiology
Kim, Leonard D.
Internal Medicine - Prelim.
Kim, Leonard D.
Surgery - Preliminary
Nene, Shriram M.
Sacramento
Univ. of CA-Davis Med. Ctr.
Surgery
Sunwoo, John B.

San Francisco
Univ. of CA-SF
Orthopedic Surgery
Fontes, Roger A.
Pediatrics
Eichner, Lora K.

Santa Monica
Santa Monica Hospital
Family Practice
Escobedo, Jodie A.

Torrance
Harbor-UCLA Med. Ctr.
Emergency Medicine
Teaford, Robert J.

COLORADO

Denver
Fitzsimmons Army Med. Ctr.
Dermatology
Wilde, Joseph L.

DISTRICT OF COLUMBIA

Washington
Howard Univ. Hospital
Surgery
Gordon, Sherilyn A.

FLORIDA

Gainesville
Univ. of FL
Ophthalmology
Kim, David D.
Jacksonville
Univ. of FL Health Sciences Ctr.
Radiology - Diagnostic
Haycocks, Ian G.

GEORGIA

Atlanta
Emory Univ. School of Medicine
Emergency Medicine
Nunge, Mark
General Surgery - Prelim.
Solomon, Joel S.
Ophthalmology
Steuer, Eric R.
Augusta
Medical College of Georgia
Orthopedic Surgery
Pellett, Jonathan B.

ILLINOIS

Chicago
Loyola Univ. Med. Ctr.
Pediatrics
Pont, Edward A.
McGaw Med. Ctr.-NW Univ.
Physical Med. & Rehab.
Cannon, Douglas T.
Rush-Presbyterian-St. Lukes
Internal Medicine - Prelim.
Levin, Michael I.
Univ. of Chicago Hospitals
Pediatrics
Davis, Michael A.

INDIANA

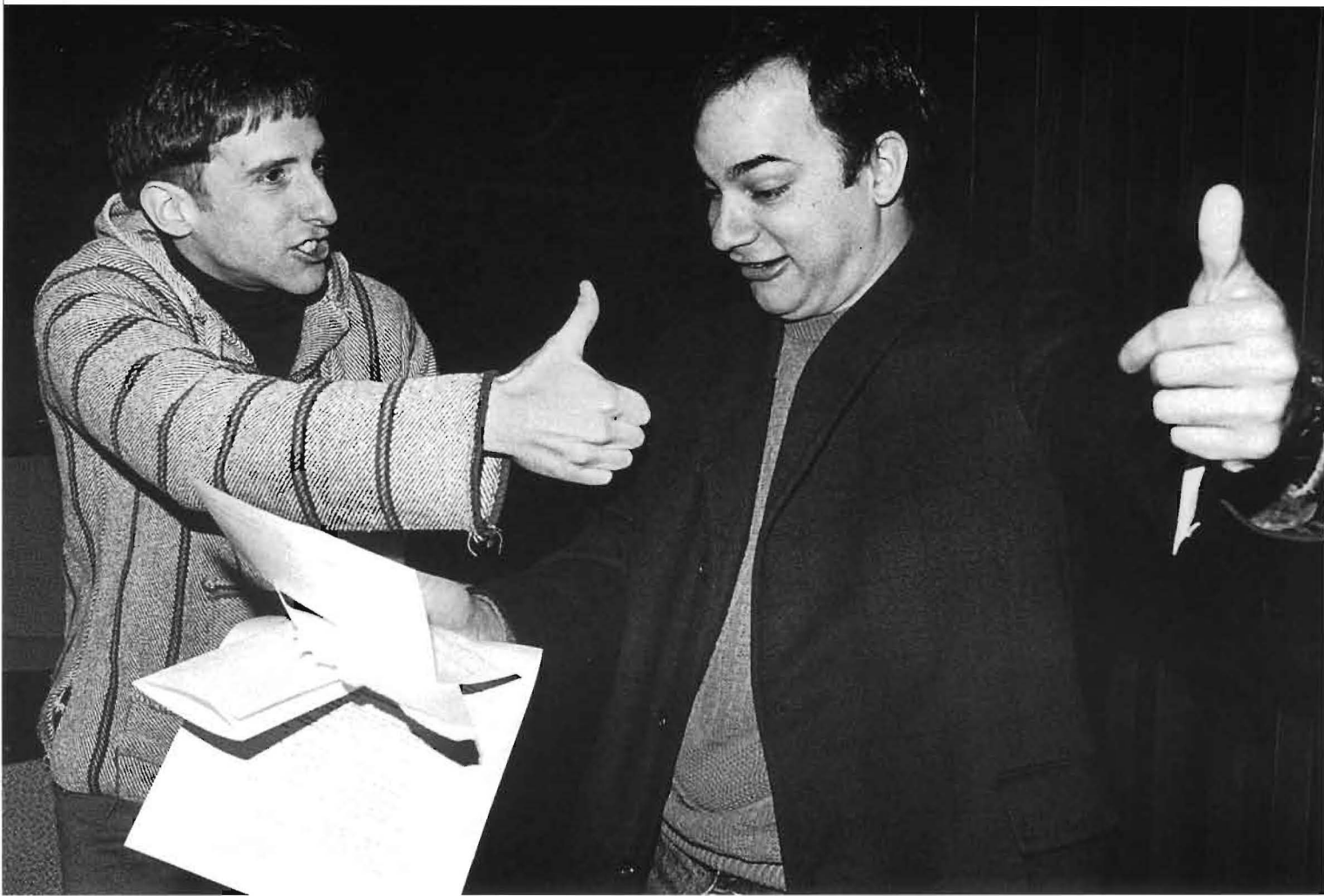
Indianapolis
Indiana Univ. Med. Ctr.
Pediatrics
Rosenman, Marc B.

KENTUCKY

Louisville
Univ. of Louisville School of Med.
Surgery
Grayson, Thomas M.

MASSACHUSETTS

Boston
Boston Univ. School of Med.
Orthopedic Surgery
Sternenberg, Paul L.
Brigham & Womens Hosp.
Internal Medicine - Prelim.
Champagne, Lynne M.
Internal Medicine
Amatruda, James F.
Ross, Theodora S.
Harvard School of Public Health
Rucker, Cheryl



Match Day results please students Seth Myles (left) and Jay Salpekar. Both will continue their training at Barnes Hospital, Myles in OB-GYN and Salpekar in psychiatry.

Harvard Mass. Gen. Hospital

Neurology
McDonald, Colin T.
Pathology
Skeleton, Timothy P.
Harvard-Longwood Area
Neurology
Champagne, Lynne M.
Simon, David K.
New England Med. Ctr.
Pediatrics
Jaeger, Jenifer L.
Fischbach, Peter S.
St. Elizabeth's Hospital
Internal Medicine
Pound, Darcie K.

MICHIGAN

Ann Arbor
Univ. of MI Hospitals
Internal Medicine
Deedy, Matthew G.

MINNESOTA

Minneapolis
Hennepin County Med. Ctr.
Family Practice
Councilman, David L.
Councilman, Robin M.
Univ. of MN Hosp. & Clin.
Internal Medicine
Crespin, Jeffrey S.
Radiology - Diagnostic
Khan, Shireen E.
Rochester.
Mayo Grad. School of Med.
Anesthesiology
Mueller, Jeff T.

MISSOURI

Columbia
Univ. Hospitals & Clinics
Family Practice
Boos, Kathleen A.

St. Louis

Barnes Hospital
Internal Medicine
Chen, Jane
Faddis, Mitchell N.
Jackson, Stephanie L.
Misir, Nahrayshwar D.
Paranjothi, Subramanian
Internal Medicine - Prelim.
McDonald, Colin T.
Obstetrics-Gynecology
Kasinak, Claudine M.
Myles, Seth A.
Orthopedic Surgery
Chough, Leo Y.
Keeney, James A.
Pathology
Densmore, Tamara L.
Psychiatry
Salpekar, Jay A.
Radiology - Diagnostic
Butman, John A.
Surgery - Preliminary
Carbone, Joseph M.

Esselman, Gregory H.
Geideman, William M.
Lin, James C.
MacDonald, Robert R.
Deaconess Hospital
Transitional
Moon, Christopher J.
Jewish Hospital
Internal Medicine - Prelim.
Bean, Joseph M.
Nemeth, Patti M.
Simon, David K.
Internal Medicine
Frenchie, Debra L.
Radiology - Diagnostic
Song, Felix L.
St. Johns Mercy Med. Ctr.
Internal Medicine
Markowitz, Scott D.
Family Practice
Eppell, Beth A.
Redmond-Norris, Cecilia M.
Transitional
Steuer, Eric R.

St. Louis Children's Hospital

Pediatrics

Cantor, Alan B.
Esselman, Tamara L.
Hanson, Robin D.
Mason, John E.
Plax, Daniel S.
Pressel, David M.
Sterkel, Randall S.
Stoszek, Renata M.
Weiner, Scott J.

Washington University

Neurology

Levin, Michael I.
Nemeth, Patti M.

Otolaryngology

Esselman, Gregory H.
MacDonald, Robert R.

Urology

Carbone, Joseph M.

NEBRASKA

Omaha

**Univ. of NE College of
Medicine**

Family Practice

Barnard, David R.

NEW JERSEY

Summit

Overlook Hospital

Transitional

Belle, Beverly A.

NEW YORK

Brooklyn

SUNY Health Sciences Ctr.

Radiology - Diagnostic

Patel, Ameet C.

Mineola

Winthrop Univ. Hosp. NY

Internal Medicine - Prelim.

Haas, Jonathan A.

New York

Long Island-Jewish

Pediatrics

Zilkha, Naomi L.

NY University

Ophthalmology

Turbin, Roger E.

Staten Island Univ. Hosp.

Internal Medicine - Prelim.

Patel, Ameet C.

Rochester

Strong Memorial Hospital

Surgery

Belin, Bruce M.

NORTH CAROLINA

Durham

Duke University Med. Ctr.

Radiation - Oncology

Bean, Joseph M.

Surgery

Magee, Kendra P.

OHIO

Cincinnati

Univ. of Cincinnati

Internal Medicine

Wright, Maria B.

Emergency Medicine

Wright, Stewart W.

Columbus

OH State Univ. Hospitals

Plastic Surgery

Bridge, Peter M.

Riverside Methodist

Family Practice

Spangler, Mark M.

PENNSYLVANIA

Philadelphia

Hosp. of Univ. of PA

Radiation - Oncology

Haas, Jonathan A.

Wills Eye Hospital

Ophthalmology

Buerger, Daniel E.

Pittsburgh

Mercy Hosp. of Pittsburgh

Transitional

Buerger, Daniel E.

Univ. of Pittsburgh

Internal Medicine - Prelim.

Gazzuolo, Debra J.

TENNESSEE

Chattanooga

Univ. of TN College of Med.

Transitional

Kim, David D.

Nashville

Vanderbilt Univ. Med. Ctr.

Internal Medicine

McKinstry, Scott W.

Orthopedic Surgery

Talwalkar, Vishwas R.

TEXAS

Dallas

Univ. of TX SW Med.

School

Internal Medicine

Conner, Blair

Gray, Joseph M.

Houston

Baylor College of Med.

Anesthesiology

Carter, James C.

UTAH

Salt Lake City

Univ. of UT Affiliated

Hosps.

Internal Medicine - Prelim.

Turbin, Roger E.

VIRGINIA

Newport News

Riverside Regional

Medical Center

Family Practice

Gasper, Kirk P.

Portsmouth

Portsmouth Naval Hospital

Pediatrics

Francoeur, Michele L.

Orthopedic Surgery

Sewell, Daniel G.

WASHINGTON

Seattle

Univ. of WA Affiliated

Internal Medicine

Cummings, Paul J.

R E U N I O N



1 9 9 3



The 1993 Reunion Award recipients (seated, left to right): Gerald T. Perkoff, M.D. '48 (Alumni Achievement Award); Henry G. Schwartz, M.D. (Distinguished Service Award) (standing, left to right): Edwin W. Salzman, M.D. '53 (Alumni Achievement Award); Ernest T. Rouse, Jr., M.D. '43 March (Alumni Faculty Award); Bernard T. Garfinkel, M.D. '48 (Alumni Faculty Award); William H. Daughaday, M.D. (Distinguished Service Award); Burton A. Shatz, M.D. '43 December (Alumni Faculty Award); Joseph M. Davie, M.D. '68 (Alumni Achievement Award).

Alumni Achievement Awards

Joseph M. Davie, M.D. '68, is vice president of research at one of the country's leading biotechnology companies, Biogen, Inc. He is also adjunct professor of microbiology and immunology at Northwestern University School of Medicine and at Washington University School of Medicine.

Davie received A.B., M.A., and Ph.D. degrees in bacteriology from Indiana University. Notably, only four years after graduation, he was named associate professor of pathology and microbiology and director of graduate studies in experimental pathology at Washington University School of Medicine. In 1975, he be-

came professor and head of the Department of Microbiology and Immunology and also professor of pathology, positions he held until 1987, when he went to Searle & Company.

Former students describe him as "a down-to-earth teacher with a genius for explaining the most complex topics in understandable terms," and "a very special person who always made time for the people he worked with, no matter how busy he was."

Gerald T. Perkoff, M.D. '48, is University Curators Professor Emeritus, Department of Family and Community Medicine, and professor of medicine at the University of Missouri-Columbia. He serves as deputy director of the Robert Wood Johnson Foundation Generalist Physicians Initiative Program.

Perkoff attended Washington University and the Washington University School of Medicine, then trained in internal medicine at the University of Utah/Salt Lake General Hospital. He moved to St. Louis in 1963 as chief of the medical service at St. Louis City Hospital, becoming professor of medicine in 1965. From 1968 to 1979, he served as founding director of the division of health care research and professor of medicine, preventive medicine and public health at the School of Medicine.

Perkoff repeatedly has been honored for his outstanding clinical teaching, both at the University of Utah School of Medicine and at Washington University School of Medicine. The University of Missouri School of Medicine designated him one of the Great

Men of Medicine in 1981.

Edwin W. Salzman, M.D. '53, is professor of surgery at Harvard Medical School and deputy editor of the *New England Journal of Medicine*. He has combined a career as a vascular surgeon with research in hemostasis and thrombosis, two concerns of surgeons who operate on blood vessels.

The son of a graduate of Washington University medical school (the late J. Marvin Salzman, M.D. '29), Salzman received the A.B. degree in 1950 and the M.D. degree cum laude from Washington University and an honorary M.A. degree from Harvard in 1969.

After his residency, Salzman climbed on the academic ladder as instructor in surgery at Harvard Medical School and the Massachusetts General Hospital,

reaching the rank of full professor in 1972.

Salzman is described as "gentle and thoughtful," "a many-faceted person whose interests outside of medicine extend from opera to sailboat racing," and "devoted to his work, his family and his friends."

Alumni/Faculty Awards

Bernard T. Garfinkel, M.D. '48, is professor of clinical medicine at Washington University School of Medicine and maintains a private practice of internal medicine.

Garfinkel obtained his M.D. degree from Washington University School of Medicine, then completed his internship and served as chief resident at Barnes Hospital. From 1951 to 1953, he served at the United States Army Armed Services Graduate School at Walter Reed Hospital and spent seven months in Korea with the Joint Military Study of Bacillary and Amoebic Dysentery.

Garfinkel returned to the School of Medicine as an instructor, moved through the ranks as assistant and associate professor and attained the rank of full professor in 1973. During many years of instructing, he has become known especially for his expertise in teaching clinical diagnosis.

Garfinkel has been described as "one of the great clinical teachers," "a fine friend," "a very compassionate clinician whose patients love him," and "a person with a lot of mental horsepower under a most benign countenance."

Ernest T. Rouse, Jr., M.D. March '43, associate professor of clinical medicine, retired in 1989 after 40 years devoted to the private practice of internal medicine.

He received his M.D. cum laude, holding the highest academic rank in his class. Rouse was a Jackson Johnson Scholar through his four years of medical school and was class president during 1942-43.

Following graduation, Rouse trained at the Mallory Institute of Pathology prior to serving as captain in the United States Army Medical Corps, European theatre, from 1943 to 1946.

Following his entrance into private practice, Rouse became director of the private medical service at Barnes Hospital. As a long-time member of the clinical faculty, he has devoted many hours to teaching.

Modest about his own achievements, he is perhaps most gratified by a tribute from a family member who designated him "husband and father cum laude." Two of Dr. and Mrs. Rouse's four children are alumni of Washington University School of Medicine.

Burton Shatz, M.D. December '43, is professor of clinical medicine and director of the Gastrointestinal Endoscopy Laboratory at The Jewish Hospital of St. Louis, responsibilities he combines with the private practice of gastroenterology.

Shatz received his A.B. and his M.D. degrees from Washington University. He completed internships at Jewish Hospital and at St. Louis City Hospital before serving as a lieutenant junior grade in the United States Navy in 1945-46. In 1949,

he became an instructor at the medical school, moved to assistant clinical professor in 1968, associate in 1973 and attained the rank of full professor in 1984.

Shatz was the first physician in the Midwest to perform colonoscopic polypectomies and to train other physicians in this procedure.

Colleagues describe him as a "pioneer in his field," and "very attentive to his patients." He has been a role model for his family as well as his students. Dr. and Mrs. Shatz's two sons are both physicians. Their daughter, Amy Sudarsky, earned her degree from Washington University and teaches at the Boston Art Institute. She is married to a physician.

Distinguished Service Awards

William H. Daughaday, M.D., is Irene E. and Michael M. Karl Emeritus Professor of Metabolism and lecturer in medicine.

Daughaday received the B.A. degree and, in 1943, the M.D. degree from Harvard Medical School. During 1949-50, he held a fellowship in biological chemistry here, working with Carl Cori. In 1951, he was named director of the metabolism division, a position he held until 1986. In 1975 he became director of the Diabetes Endocrinology Research Center and from 1978 to 1987 he was director of the Diabetes Research and Training Center. Daughaday was named Irene E. and Michael M. Karl Professor of Metabolism in 1983 and emeritus professor in 1988.

He is best known for his discovery of insulin-like

growth hormones, or somatomedins, from which he developed a central organizing concept in modern endocrinology.

Those who have studied and worked with Daughaday are singularly devoted to him and describe him as "a sage counselor," someone who is "deeply committed to the welfare of his students," and who has "displayed outstanding citizenship throughout his career at the medical school."

Henry G. Schwartz, M.D., is August A. Busch, Jr. Professor Emeritus and lecturer in neurological surgery.

He received the B.A. degree from Princeton University and the M.D. degree from Johns Hopkins in 1932. He spent two years as a fellow at Harvard Medical School, becoming an instructor in anatomy. In 1936, he accepted a fellowship in neurological surgery here and trained with Ernest Sachs, beginning a career that led to becoming head of the Department of Neurological Surgery, a position he held for 28 years.

Schwartz set up a residency training program that is legendary for its rigorous standards. Characterized by a dual emphasis on research and clinical skills, the program produced neurosurgeons trained in surgery, basic anatomy and pathology and with a background in basic or clinical research on the nervous system. Many of those trained by Schwartz have gone on to direct training programs at other institutions.

His associates describe him as a "model of excellence," and "an avid fisherman and lover of nature as well as his fellow man." ■

The Classes Of 1943

On September 1, 1939, Hitler opened his blitzkrieg on Poland. That same week, the School of Medicine admitted a new class of students. Accelerated because of the ensuing war and the critical need for doctors, those students graduated in March of 1943. The class that entered a year later went to school for two summers and graduated in December of 1943. Because they spent so much uninterrupted time together, these classes always have shared a special camaraderie that is partly friendly rivalry. A special salute to members of the Classes of 1943 who studied and served under such difficult conditions.



Reunion-goers from the Class of March, 1943. (Front row) Leonard Kent, Warren Bowersox, Grace Bergner, Denise Quinn, Wilma Shields, A. Paul Naney, Harlan Firminger (second row) Ernest Rouse, Jr., Richard Yore, William Seidler, James Read, John Arthur, Raymond Charnas, Irvin Mattick, Harry Wittler (top row) Carlton Watkins, G. Russell Aufderheide, William Klingberg, Dallas Anthony, Henry Uhlemeyer, Frank Wissmath, David Feldman, Leslie Rose and Gordon Todd.



Reunion-goers from the Class of December, 1943. (Front row) Richard Jones, Robert Tichenor, Alva (Ace) Trueblood, Louis Gottschalk, Herbert Wiegand, James Vest (second row) Saul Silvermintz, Edward Czebrinski, W. Hammond Jones, Alvin Goldfarb, Frances Chappell Wilson, William Middleton, Terrell Covington, Jr. (third row) Norman Asel, James Cravens, Morris Alex, Thomas Stauffer, Edwin Krebs, Walter Kennedy, Burton Shatz, Stanley Moore (fourth row) John Eisenhower, John Wilson, William Miller, David Krebs, Carl Woolsey, H. Lawrence Allred, James Tagge, Tod Makley, Edward Kowert (top row) Harold Walters, Donald Smith, Conrad DeBold, Harry Lichtwardt, Jack Ingram, James Haddock, Glenn McElroy, Jerry Allen, Jr., and C. Read Boles. Not pictured is David Stadtner.



From the March contingent, Grace Bergner, M.D. '43 March, Wilma Shields, M.D. '43 March, and Denise Quinn, M.D. '43 March.



Tod Makley, M.D. '43 December and Virginia Donley, widow of Leo F. Donley, Jr., M.D. '43 December.



Eleanor Rouse, Elizabeth Danforth, Bernard Garfinkel, M.D. '48, and Judith Garfinkel socialize.



Ernest Rouse, Jr., M.D. '43 March, and Eleanor Rouse.



Tom Stauffer, M.D. '43 December, visits with Nobelist Edwin Krebs, M.D. '43 December.



Betsy Michael and James Michael, M.D. '53.



Jo Koehler, Matt Becker, M.D. '58, and Glenn Becker share a light moment.



Naomi Silvermintz and Saul Silvermintz, M.D. '43 December, are shown in front of the class pictorial history.



David Stabenow, M.D. '68, Penny Shackelford, M.D. '68, and Gary Shackelford, M.D. '68.



Ira Kodner, M.D. '67, Barbara Kodner, W. Hammond Jones, M.D. '43 December, and Polly Jones share a table.



Executive Vice Chancellor Willam A. Peck, M.D., presents the Alumni Achievement Award to Joseph Davie, Ph.D., M.D. '68.



Nancy Ebsen and William Daughaday, M.D.



Roger Fontes, Lora Eichner, Robert MacDonald, Lynne Champagne, Jonathan Haas, Claudine Kasinak and Daniel Buerger ably represent the Class of '93.



Dorothy Rinderer pins a corsage on Mardelle Krebs.



Arthur Oberman, M.D. '58 and Reba Oberman.



Carl Woolsey, M.D. '43 December shakes the hand of C. Read Boles, M.D. '43 December.



Ansel Marks, M.D. '53 and Ellis Taylor, M.D. '53.



Robert MacDonald, president of the Class of '93, responds to the welcome of his class into WUMCAA.



Outgoing president of the WUMCAA, Penny Shackelford, M.D. '68, presents the gavel to Barry Siegel, M.D. '69, incoming president.



Henry Schwartz, M.D., Patricia Peck and Willam A. Peck, M.D., converse.



Audrey Shatz and Burton Shatz, M.D. '43 December.



Paul Webber, M.D. '78, Jeff Milbrandt, Ph.D., M.D. '78, and John White, M.D. '78, reminisce at the Thursday night welcoming party.



Cheryl Rucker and Kendra Magee, both members of this year's class.



Mary Evalyn Wulff and George Wulff, Jr., M.D. '33.



Allen Pepple, M.D. '33, Russell Blattner, M.D. '33, Edna Sakimoto, Richard Sakimoto, M.D. '33, and Eda Sakimoto-Iinuma.



Stanley Korsmeyer, M.D., and Philip Majerus, M.D. '61, led a tour of a hematology lab in the Clinical Sciences Research Building. Attending were: Harlan Firminger, M.D. '43 March, Jack Ingram, M.D. '43 December, Alex Mueller, M.D. '38, George Blankenship, M.D. '38, and Mark Austin, M.D. '83.



Bitsy Loewenstein and Joseph Loewenstein, M.D. '63, chat with Laurence Jacobs, M.D.



John White, M.D. '78, Kathleen Kent and Harold Kent, M.D. '78.



Carl Denison, M.D. '68, Lynn Taussig, M.D. '68, and Vernon Loverde, M.D. '68.



Edwin Salzman, M.D. '53, with his wife, Nancy Salzman, his mother, Mrs. J. Marvin Salzman, and his son, David Salzman, Ph.D.



James Hesper and Emily Smith, M.D. '68.



Robb Ohtani, M.D. '83, Jay Ponder, and Dawn Groten-Stapleton, M.D. '83.



The solemnity and the joy of graduation day can be read on the faces of Matthew Deedy and Lynne Champagne as they take part in the School of Medicine's commencement exercises. On May 14, the school conferred 11 M.D./Ph.D. degrees, two M.D./M.A. degrees and 83 M.D. degrees.

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St. Louis, MO 63110-1093



After Jack Watkins' hand was severed and re-attached at the wrist, he told his therapists how much he missed his beloved pastime of fishing. Occupational therapists at the School of Medicine devised an attachment for the splint Watkins wore that let him use rod and reel, and he was back fishing within two weeks of his injury. That outcome met his functional goals and sped his physical and emotional healing. Incidents like this have occurred in occupational therapy departments for three-quarters of a century. On May 6 and 7, the Program in Occupational Therapy celebrated its 75th anniversary, tracing its roots to the first program established west of the Mississippi. In 1919, the first graduating class comprised 10 members. This year, the program graduated 73 occupational therapy students.